## REMARKS

After entry of the amendment, claims 50, 69, 70, and 73-98 are pending. Claims 1, 48, 60, 68, 71-72 have been canceled, and new claims 78-98 have been added.

Support for the claim amendments is provided, *e.g.*, as follows: claim 50: p. 34, line 8 (*in vitro*) and original claim 59 (reinstated as claim 71) (tissue sample); and, claim 69: p. 35, lines 11-15, original claim 30, p. 35, lines 8-10. Support for the new claims is provided throughout the specification, *e.g.*, as follows: new claims 78, 83, and 96: p. 34, lines 8-10; new claims 79, 80, 84, 89, 97, and 98: table 16, p. 97 (examples of monoclonal antibodies); new claims 81 and 85-87, and 91: p. 34, line 22 to p. 35, line 15; new claims 82 and 92: p. 35, lines 8-10; new claims ; new claim 93: p. 34, lines 4-6; new claim 94: p. 34, lines 15-17; and, new claim 95: p. 34, lines 4-5.

### Amendments to the Specification

The specification has been amended to conform to replacement Figures 15A-15E. The amendment to the instant specification was required because it is a copy of the specification of the parent application, which briefly described a single Figure 15, not Figures 15A-15E as were filed with the instant application.

The paragraph beginning on page 8, line 32, has been replaced with six replacement paragraphs. The replacement paragraphs describe Figures 15A-15E, 15A, 15B, 15C, 15D, and 15E, respectively. The paragraph beginning on page 67, line 27, has been amended to disclose the correct alum concentration. Support for the amendments to the specification can also be found in informal Figure 15 of USSN 09/201,430, filed November 30, 1998, which is incorporated herein by reference. Thus, the amendments to the specification contain no new matter.

Applicants address the Examiner's remarks using the paragraph numbering of the office action.

2. Sequence Listing

The office action states that Figures 19 and 20 of the application contain 42 separate sequences and that the sequence listing and amendment of September 11, 2001, which refer to SEQ ID NOS:1-41 for these figures, lack at least one sequence identifier.

However, the sequences in the thirty second and thirty third positions in Figures 19 and 20 have the common amino acid sequence VGSNKGAIIG, and are both represented by the sequence identifier SEQ ID NO:32. Thus the amendment and sequence listing filed September 19, 2001 comply with 37 CFR 1.821-1.825.

3. Drawings

Amendments to Figure 11

Figure 11 has been amended to add a legend. Support for this amendment can be found from page 62, line 25 to page 64, line 2 of the instant application.

Amendments to Figures 15A-15E

Figure 15D as filed in the instant application discloses an alum concentration of 2μg/ml. The replacement Figure 15D discloses an alum concentration of 2 mg/ml. Figures 15A-15E have been amended to correct an obvious error; "p Malue" has been replaced with "p Value." Support for both of these amendments is provided by the informal Figure 15 as originally filed in the parent application. Therefore, the amendments to the figures contain no new matter.

Amendments to Figure 16

The descriptive term "Anti AB" has been replaced with the term "Anti-Abeta" to give greater clarity to the title. Support for this amendment can be found on page 92, lines 28-33 of the instant application.

4. IDS

Applicants' citation of the references has included all the elements required to comply with 37 C.F.R. §§ 1.97-98 that are known to them.

5. Applicants acknowledge that the Group III claims have been elected.

6. Withdrawn claims have been cancelled.

7-8. The claims stand provisionally rejected for same invention double patenting against claims 91-100 of copending application 09/979,701 and claims 50-59 of 09/724,552, 09/724,273, 09/724,551. Claims 50-59 have been canceled in Application Nos. 09/724,552, 09/724,273, and 09/724,551, thus mooting the rejection. Applicants propose the provisional rejection of claims 50-59 against claims 91-100 of Application No. 09/979,701 remain in abeyance until indication of otherwise allowable subject matter. By this time, claims 91-100 of Application No. 09/979,701may be different due to restriction requirements , election of species requirements or other reasons.

9. Claim 70 stands rejected as in improper dependent form for failing to further limit its antecedent. The claim 70 has been amended to clarify that the claim specifies an order of combining reagents.

10-12. Claim 50 stands rejected as indefinite in referring to an "antigen-associated biological entity" a "biological entity" and "physically associated," This rejection has been mooted by amendment of the claim to refer to a tissue sample. The objected-to terms are no longer used.

13. Claim 50 also stands rejected due to alleged inconsistency between the preamble and end step. This rejection is moot in that the claim has been amended so that both the preamble and end step refer to a tissue sample.

14. Claim 69 is rejected as indefinite in that it recites monitoring an amount of antigen, whereas claim 50 refers to monitoring an "antigen-associated biological entity." Claim 69 has been amended to clarify that the amount of tissue sample (as now recited in claim 50) is monitored by monitoring the amount of an antigen associated with the tissue sample.

15. Claims 73, 74 and 77 are alleged to lack antecedent basis for "tissue sample." However, antecedent basis is provided by amended claim 50.

16-17. Claims 50, 69-72 and 77 stand rejected as allegedly anticipated by Jorbeck under 35 USC 102(b). Jorbeck is alleged to teach *in vivo* and *in vitro* assays in which polyclonal sera and phagocytic cells are tested for capacity to phagocytose Salmonella. This rejection is respectfully traversed as applied to the amended claims.

Jorbeck does not disclose or suggest testing an antibody for capacity to clear a tissue sample *in vitro* as specified in the amended claims. A tissue comprises an "aggregation of similarly specialized cells united in the performance of a particular function" (*see* Dorland's Illustrated Medical Dictionary (27th ed, Sanders, 1988)). By contrast, Jorbeck analyzes a suspension of individual nonspecialized cells, namely Salmonella. Jorbeck's alleged observation of clearing of such individuals cells does not suggest that one could or should attempt to clear a tissue sample *in vitro* as a means of screening an antibody. Jorbeck particularly does not disclose or suggest screening an antibody for capacity to clear any of the types of tissue recited in claim 77. For these reasons, withdrawal of the rejection is respectfully requested.

Jorbeck does not disclose or suggest testing an antibody for capacity to clear an isolated biological entity as specified in new claim 81, a biological entity physically associated with an antigen as specified in new claim 87, or an amyloid deposit as specified in new claim 90. Thus, new claims 81, 87, and 90 and the claims respectively depending therefrom are not anticipated by Jorbeck under 35 USC 102(b).

18. Claims 50 and 69-77 stand rejected as allegedly anticipated by Vitek, US 5,935,927. It is alleged that Vitek teaches screening for the effectiveness of an advanced

glycosylation end product bearing targeting agent *in vitro* and *in vivo* (citing to paragraph bridging cols. 21 and 22, col. 24, lines 13-24, and col. 22, line 54 to col. 23, line 4). Such assays are alleged to include a combination of an anti-AGE antibody, various antigens including Aβ and phagocytic cells. This rejection is respectfully traversed as applied to the amended claims.

Insofar as Vitek is alleged to provide disclosure of *in vivo* assays, such disclosure is moot in view of amendment of the claims to specify that components of the assay are combined *in vitro*.

Further, Vitek does not disclose an *in vitro* assay in which an antibody is screened for clearing activity, as claimed. In Vitek's *in vitro* assay, the object is not to screen an antibody but rather to screen AGE -TF (thioflavin) for capacity to modify insoluble or aggregated Aβ (col. 22, lines 53-55). This is achieved by the following steps. First, AGE-TF is contacted with aggregated Aβ. The incorporation of AGE-TF into aggregated Aβ is then tested by ELISA using an antibody (col. 22, lines 58-61). The antibody in this step is used simply as a conventional diagnostic reagent, and is not itself being screened for anything. After verifying incorporation of AGE-TF, phagocytic cells are added to test for clearance of AGE-TF modified Aβ (col. 22, lines 61-65). However, at the time the phagocytic cells are added, there is no indication that the antibody used for the ELISA is still present. It would be most logical and typical practice when performing a diagnostic step on an intermediate product in a process to perform the diagnostic step on only a sample of the intermediate so as to avoid influencing the further processing of the intermediate by contamination with the reagents in the diagnostic step. In any event, insofar as there is doubt as to whether Vitek proposes adding phagocytic cells to the same or a different vessel to that in which the ELISA using antibody to AGE-TF is performed, that doubt should inure to the benefit of applicants given that the burden of proof rests on the PTO (*In re Piasecki*, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984)).

For these reasons, Vitek's method differs from that claimed at least in that Vitek does not disclose simultaneous presence of an antibody and phagocytic cells in an *in vitro* clearing reaction, nor that the clearing reaction screens an antibody for clearing activity. Withdrawal of the rejection is respectfully requested.

For the same reasons discussed above, new claims 81, 87, and 90 and the claims respectively depending therefrom are not anticipated by Vitek.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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